

# Anlage D1

PCT

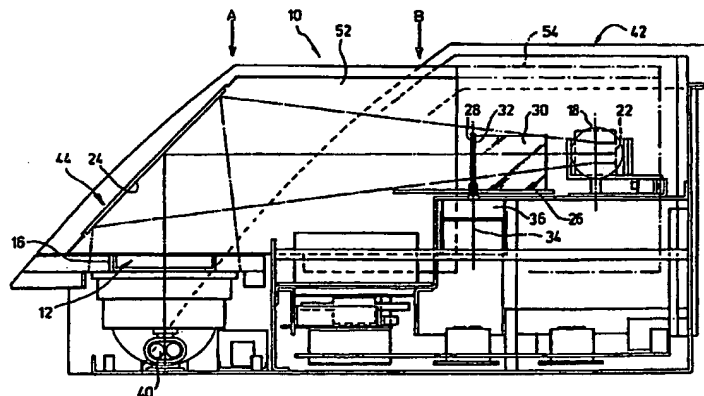
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## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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<p>(21) International Application Number: <b>PCT/GB93/02262</b> (22) International Filing Date: <b>3 November 1993 (03.11.93)</b> (30) Priority data: <b>9223259.4 6 November 1992 (06.11.92) GB</b> (71) Applicant (for all designated States except US): <b>QUATRO BIOSYSTEMS LIMITED [GB/GB]; Broadoak Business Centre, Ashburton Road West, Trafford Park, Manchester M17 1RW (GB).</b> (72) Inventors; and (75) Inventors/Applicants (for US only): <b>MOORE, Robert, John, Frank [GB/GB]; The Hollies, 13 Croft Road, Wilmslow, Cheshire SK9 6JJ (GB). McCULLOCH, Peter, Frederick [GB/GB]; 54 Hawthorn Lane, Wilmslow, Cheshire SK9 5DQ (GB). WHITESIDE, Melvyn, Christopher [GB/GB]; 107 Castle Green, Westbrook, Warrington WA5 5XB (GB).</b></p>		<p>(74) Agents: <b>GODDARD, David, John et al.; Dibb Lupton Broomhead, Carlton House, 18 Albert Square, Manchester M2 5PE (GB).</b> (81) Designated States: <b>US, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).</b> <b>Published</b> <b>With international search report.</b></p>

### (54) Title: METHOD AND APPARATUS FOR IMAGE ANALYSIS



### (57) Abstract

A method and apparatus are described for the analysis of a sample image, e.g. as in blood-typing. The method comprises the steps of presenting the sample image to a single black and white camera, viewing the sample image by said black and white camera sequentially through at least two colour filter means interposed in the optical path between the sample image and the camera; digitising and storing in computer memory means a grey scale picture from the output of said camera after viewing the sample image through each of said at least two colour filter means; analysing by computer program means at least one of said stored digitised camera picture outputs of the sample image to determine positional data of physical shape elements of said sample image; combining said at least two grey scale pictures in said computer memory means by computer program means to form a composite grey scale picture of said sample image; assigning a value to each shade and allocating a specific colour to each of said values in said composite grey scale picture from a range of chosen colours stored in said computer program to generate a colour picture of said sample image.

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#### METHOD AND APPARATUS FOR IMAGE ANALYSIS

The present invention relates to a method and apparatus for the analysis of images particularly, though not exclusively, of images associated with the analysis and testing of organic samples.

The analysis of human blood to establish its type is based on a technique known as agglutination. In one application of this technique a sample plate comprising a series of sample wells each containing a small quantity of, for example, a patient's blood, have various reagents added to each well to establish a particular characteristic of that patient's blood. Each well will produce a result which has visual characteristics of colour and physical appearance depending upon the reaction of the reagent with the blood in each well. A reaction between the reagent and the blood sample in a well may produce for example, an agglomeration of the red blood cells to produce a relatively small and discreet clump of material having a particular shade of red in the bottom of the well. Another reaction may, for example, produce a relatively large area of a uniform deposit or precipitate (sometimes referred to as a "lawn") having a uniform colour density. Yet other reactions may produce deposits or precipitates having a granular appearance and being of a shade of orange for example.

A typical sample plate may, for example, have a matrix of wells comprising eight rows of twelve wells, each row of twelve wells having a sample of blood from a single patient. Each row will have a reagent added to each succeeding well in a particular and predetermined order. It is the pattern of reactions in each succeeding well which determines the blood type of the patient from whom the blood in that row was taken.

There are several methods which have been employed heretofore to "read" the pattern of reactions and so establish the blood type. One method is for a skilled person to physically view the sample plate and make an assessment based on skill and experience. Clearly this method has many inherent disadvantages including variation from one person to another, and the likelihood of pure human error in the assessment.

Another technique which is used is that of photometric analysis but this technique has the principal disadvantage that it can only provide a limited amount of the information which is available in any individual well. This is because only single line scanning is used; multiple line scanning not being practicable due to the excessive time which would be required to scan the complete area of each well. A further disadvantage stems from the fact that typical beam width is about 2.5mm giving significant overlap of adjacent fields at each scan position, therefore confusing the information at adjacent scan sites and giving poor resolution.

Yet another method of reading the sample plate is by image analysis using a colour camera in conjunction with a computer software program. One problem with the use of a colour camera is that to obtain a high level of resolution to determine the physical shape characteristics of a deposit, the cost of such cameras is very high. A second problem, also associated with resolution, is that each piece of colour information within the generated image produced from a colour camera is the result of the combination of three pixels. A pixel is, simply stated, an individual picture element produced by the camera, and to produce a colour shade, a combination of four pixels including one each of a red, blue and green pixel is required to produce one corresponding colour spot in an image. Therefore, if an area of an image comprises 1200 pixels, for example, only 300 "spots" of colour information will result in the picture produced with a colour camera. This results in direct reduction in resolution of a factor of four.

It is an object of the present invention to provide a method for the analysis of a colour image and an apparatus for carrying out that method which will not have the disadvantages of high cost and relatively poor resolution of the prior art methods and equipment.

According to a first aspect of the present invention there is provided a method for the analysis of a sample image having elements of colour and shape, the method comprising the steps of presenting the sample image to a single black and white camera; viewing the sample image by said black and white camera

sequentially through at least two colour filter means interposed in the optical path between the sample image and the camera; digitising and storing in computer memory means a grey scale picture from the output of said camera after viewing the sample image through each of said at least two colour filter means; analysing by computer program means at least one of said stored digitised camera picture outputs of the sample image to determine positional data of physical shape elements of said sample image; combining said at least two grey scale pictures in said computer memory means by computer program means to form a composite grey scale picture of said sample image; assigning a value to each shade of grey in said composite grey scale picture; and allocating a specific colour to each of said values in said composite grey scale picture from a range of chosen colours stored in said computer program to generate a colour picture of said sample image.

In one embodiment of the method of the present invention, there are three colour filter means comprising a red, a blue and a green colour filter. The image to be analyzed is viewed consecutively by a single black and white camera through each separate colour filter. As the image is viewed in turn through each colour filter, a first computer program means generates a grey scale computer "picture" which is stored in computer memory means. The three grey scale computer "pictures" when combined result in each element of the image being viewed having assigned to it a value between 0 and 255. 8-bit digitisers give a range of 256 different shades of grey. Each different shade of grey has a specific colour assigned to it by a second computer program

means which analyses the final combined computer "picture". The second computer program means has the necessary software to analyze the "picture" produced in terms of colour and shape characteristics of deposit or precipitate to determine the blood type in a row of sample wells in a sample plate. Thus, an accurate colour representation is displayed on a monitor screen for viewing and analysis.

It should be understood that although the computer program means have been distinguished as first and second program means to identify the functions that they perform, they may exist together in a single computer program software package. Similarly, such a software package will also typically include program software relating to controlling the sequence of steps which the apparatus carrying out the method will perform whilst producing an image analysis.

A particular advantage of the system of using separate colour filters in conjunction with a black and white camera is that each pixel of information is used to build the picture image in terms of shape characteristics, thus producing a particularly high resolution to determine small detail in samples being analyzed.

According to a second aspect of the present invention there is provided apparatus for carrying out the analysis of a sample image having elements of colour and shape, the apparatus comprising means for receiving said sample image to be analyzed; single black and white camera means for viewing said sample image; at least two colour filter means sequentially interposable

in the optical path between said sample image and said camera means; computer program means for digitising the output from said camera means for forming a grey scale picture of said sample image after viewing through each of said at least two colour filter means; computer memory means for storing said digitised grey scale pictures; computer program means for analysing at least one of said grey scale pictures to determine positional data of physical shape elements of said sample image; computer program means for combining said at least two grey scale pictures in said computer memory means to form a composite grey scale picture of said sample image; and computer program means for allocating a specific colour to each shade of grey in said composite grey scale picture.

The image to be viewed may be a sample plate having reacted blood samples in the wells thereof. Such reacted samples are frequently very delicate and are disturbed by vibration and movement thereby possibly altering the visual shape characteristics of the deposit or precipitate and leading to an erroneous result. In one embodiment of the apparatus of the present invention the image is viewed by the camera through a movable mirror thereby allowing the image to remain stationary and prevent any physical deterioration of the actual sample. In prior art apparatus, the sample is generally moved into and out of the camera viewing field or optical path.

The apparatus of the present invention may also have computer program means to control the sequence of events during the analysis of an image. Again, as stated above all of the computer



program means may be combined into a single integrated computer software package to provide all the computer functions required.

It must be most emphatically stressed that although the present invention has been described above with regard to the analysis of blood as in blood typing, the method and apparatus are equally applicable to the analysis of many other images having elements of colour and/or shape. In the field of medicine, for example, the invention may be used for analysing the results of tests for HIV, hepatitis and many others. The invention has potential application in many other fields such as, for example, organic chemistry, metallurgy where colour and/or shape analyses are frequently required.

In order that the present invention may be more fully understood, an example will now be described by way of illustration only with reference to the accompanying drawings, of which:

Figure 1 shows a line drawing in elevation of an apparatus according to the present invention;

Figure 2 shows a plan view of the apparatus of Figure 1;

Figure 3 shows a schematic flow diagram relating to the major apparatus features; and

Figure 4 which shows a schematic flow diagram of the steps in the analysis of a sample image.

Referring now to the drawings and where the same features are denoted by common reference numerals. The apparatus is indicated generally at 10 and the following description is to be understood as an example only which refers specifically to the case where blood typing is being carried out. A sample plate 12 having a matrix of eight rows of twelve individual sample wells 14 is placed in a sample plate receiving tray 16 at the front of the apparatus. A black and white television camera 18 is mounted to the rear of the apparatus at a level above that of the sample plate 12. The camera 18 views the plate 12 by means of two mirrors 22, 24. The first mirror 22 turns the field of view laterally through 90°, and the second mirror 24, positioned above the plate 12, turns the field of view vertically through 90°. The angle of view of the camera 18 is such that the whole surface area of the sample plate 12 may be viewed by the camera. Interposed between the camera 18 and the sample plate 12 is a carousel 26 having three colour filters red 28; blue 30; and green 32 each set in 90° steps. The carousel 26 rotates about a vertical axis 34 and is driven by a synchronous motor 36. Thus the camera is able to view the sample plate directly or through one of the coloured filters 28, 30 or 32 depending upon the position of the carousel. The sample plate 12 is made of transparent material and is illuminated by a "white" light source 40 positioned below. The apparatus elements described above are contained within a casing indicated generally at 42 and which is so constructed as to exclude ambient light whilst the sample plate is being viewed by the camera. At the front of the casing 42 is a slidable door 44 which is driven by a rack 46 and pinion 48 from a drive motor 50 and traverses in a horizontal plane. The

door 44 has the second mirror 24 mounted on the inside thereof and is indexable between two positions indicated by the arrows "A" and "B" (see Fig.1). The door 44 has sidewalls 52 so as to exclude ambient light when in position "A". It is when the door 44 is in position "A" that the camera views the sample plate 12 as the mirror 24 is then positioned above the samples. When the door is in position "B" (indicated by dashed lines 54), the sample plate 12 may be placed in or withdrawn from the receiving tray 16. Also mounted within the apparatus are computer elements in the form of cards (indicated at 60) which have inputs from the camera 18 and which have outputs to control the sequence of the various moving elements of the apparatus. The apparatus also includes a monitor display driver and computer memory means (also in card form 60) to store the analyses of test samples for subsequent recall. The apparatus also includes an external colour monitor. Other devices such as printers (not shown) and plotters (not shown) may also be employed as additional or alternative methods of displaying results. A keyboard may also be utilised for inputting information or determining how the apparatus functions.

The interrelationship between the major apparatus features are indicated schematically in Figure 3.

In operation the apparatus described above functions in the following manner. The sample plate 12 is placed in the tray 16 and the computer program drives the door 44 out into position "A" to cover the plate and rotates the carousel 26 to position the red filter 28 into the field of view between the camera 18 and

the sample plate 12. This allows only red light to reach the camera and the output from the camera to the computer causes the image of the plate 12 to be recorded in the computer memory, the output of the camera having been digitised by the computer and an 8 bit (256 level) grey scale image appears on the monitor screen. The computer software reads the value of each of the pixels of light on the screen sequentially, extracts the most significant 3 bits of data and transfers them to the computer memory in the same pattern as they appear in the sample plate 12 and on the monitor screen. The motor 36 then indexes the carousel 26 to interpose the blue filter 30 into the camera field of view so that only blue light is transmitted to the camera. Again, an 8 bit (256 level) grey scale image appears on the monitor screen. The software reads the value of each of the pixels sequentially, extracts the most significant 2 bits of data and transfers them to the computer memory in the same pattern as they appear in the sample plate 12 and on the monitor screen. This process is again repeated with the green filter and the most significant 3 bits of data are extracted and transferred to computer memory in the same physical pattern as they appear in the sample plate and on the screen. The computer program allocates a range of chosen colours in a palette from the full range of available colours, in this case 256,000 colours, to the 256 available colours in the 8 bit system. For example, the display colour 128 could be set to a shade of light blue, 12 to a dark shade of grey and 200 to a shade of yellow. The actual shades of colours may be chosen to concentrate colour discrimination in the green and red parts of the spectrum which is particularly relevant to blood typing. Similarly, the colours chosen for the colour palette may be

specifically chosen to suit any particular analysis or sample image in question. The composite computer "picture" of the three combined digital computer grey scale "pictures" is copied into a video RAM in blocks where it appears in the allocated colours on the monitor screen. Computer software then reads the colour "picture" to determine the blood type for each row of wells 14. Alternatively, the computer program may analyze one or more of the digitised grey scale pictures stored in the computer memory to determine the nature or type of the samples in the wells 14 of the sample plate 12.

Figure 4 indicates the analysis steps carried out and as described above.

Clearly many modifications may be made to the choice and arrangement of components in the apparatus described above without departing from the invention.

Although the apparatus as described in the example employs three different coloured filters, it may be desirable in some applications to use only two filter colours if the colours in the sample image to be analyzed lie in specific limited areas of the colour spectrum.

As an alternative to white light described in the above embodiment, an ultra violet light source may be used to determine the presence of fluorescent materials in the sample to be analyzed.

The apparatus described above uses transmitted light to illuminate the sample image. However, in some applications such as the examination of a metallurgical microstructure for example, reflected light must be used. The apparatus may therefore be suitably modified to employ reflected light.

Similarly, appropriate computer software may be produced for each desired image analysis application which the method and apparatus of the present invention are required to perform.

CLAIMS

1. A method for the analysis of a sample image having elements of colour and shape, the method comprising the steps of presenting the sample image to a single black and white camera; viewing the sample image by said black and white camera sequentially through at least two colour filter means interposed in the optical path between the sample image and the camera; digitising and storing in computer memory means a grey scale picture from the output of said camera after viewing the sample image through each said at least two colour filter means; analysing by computer program means at least one of said stored digitised camera picture outputs of the sample image to determine positional data of physical shape elements of said sample image; combining said at least two grey scale pictures in said computer memory means by computer program means to form a composite grey scale picture of said sample image; assigning a value to each of said values in said composite grey scale picture; and allocating a specific colour to each shade of said values in said composite grey scale picture from a range of chosen colours stored in said computer program to generate a colour picture of said sample image.
2. A method according to claim 1 wherein there are 3 colour filter means comprising red, green and blue.
3. A method according to either claim 1 or claim 2 wherein the colour picture is displayed on a colour monitor.

4. A method according to any one preceding claim wherein said colour picture is stored by computer disc means.
5. A method according to any one preceding claim wherein at least one of said at least two grey scale pictures in said computer memory means is analyzed by computer program means to determine the elements of colour and shape in said sample image to determine the type or nature of said sample.
6. A method according to any one preceding claim wherein said sample is of human or animal origin.
7. A method according to claim 6 wherein said sample is blood.
8. A method according to any one preceding claim wherein said sample image comprises a sample plate having a plurality of individual sample wells.
9. A method according to claim 8 wherein all sample wells are viewed simultaneously by said single black and white camera.
10. A method according to any one preceding claim wherein said range of chosen colours comprises 256 colours.
11. A method according to claim 1 wherein said generated colour picture of said sample image is analyzed by computer program means to determine the type or nature of said sample .



12. A method according to any one preceding claim wherein said sample image is illuminated by transmitted white light.
13. A method according to any one of preceding claims 1 to 11 wherein said sample image is illuminated by transmitted ultra violet light.
14. A method according to any one of preceding claims 1 to 11 wherein said sample image is illuminated by reflected light.
15. Apparatus for carrying out the analysis of a sample image having elements of colour and shape, the apparatus comprising means for receiving said sample image to be analyzed; single black and white camera means for viewing said sample image; at least two colour filter means sequentially interposable in the optical path between said sample image and said camera means; computer program means for digitising the output from said camera means for forming a grey scale picture of said sample image after viewing through each of said at least two colour filter means; computer memory means for storing said digitised grey scale pictures; computer program means for analysing at least one of said grey scale pictures to determine positional data of physical shape elements of said sample image; and computer program means for combining said at least two grey scale pictures in said computer memory means to form a composite grey scale picture of said sample image;

computer program means for allocating a specific colour to each shade of grey in said composite grey scale picture.

16. Apparatus according to claim 15 further including colour monitor means.

17. Apparatus according to either claim 15 or claim 16 further including mirror means by which said sample image is viewed by said black and white camera.

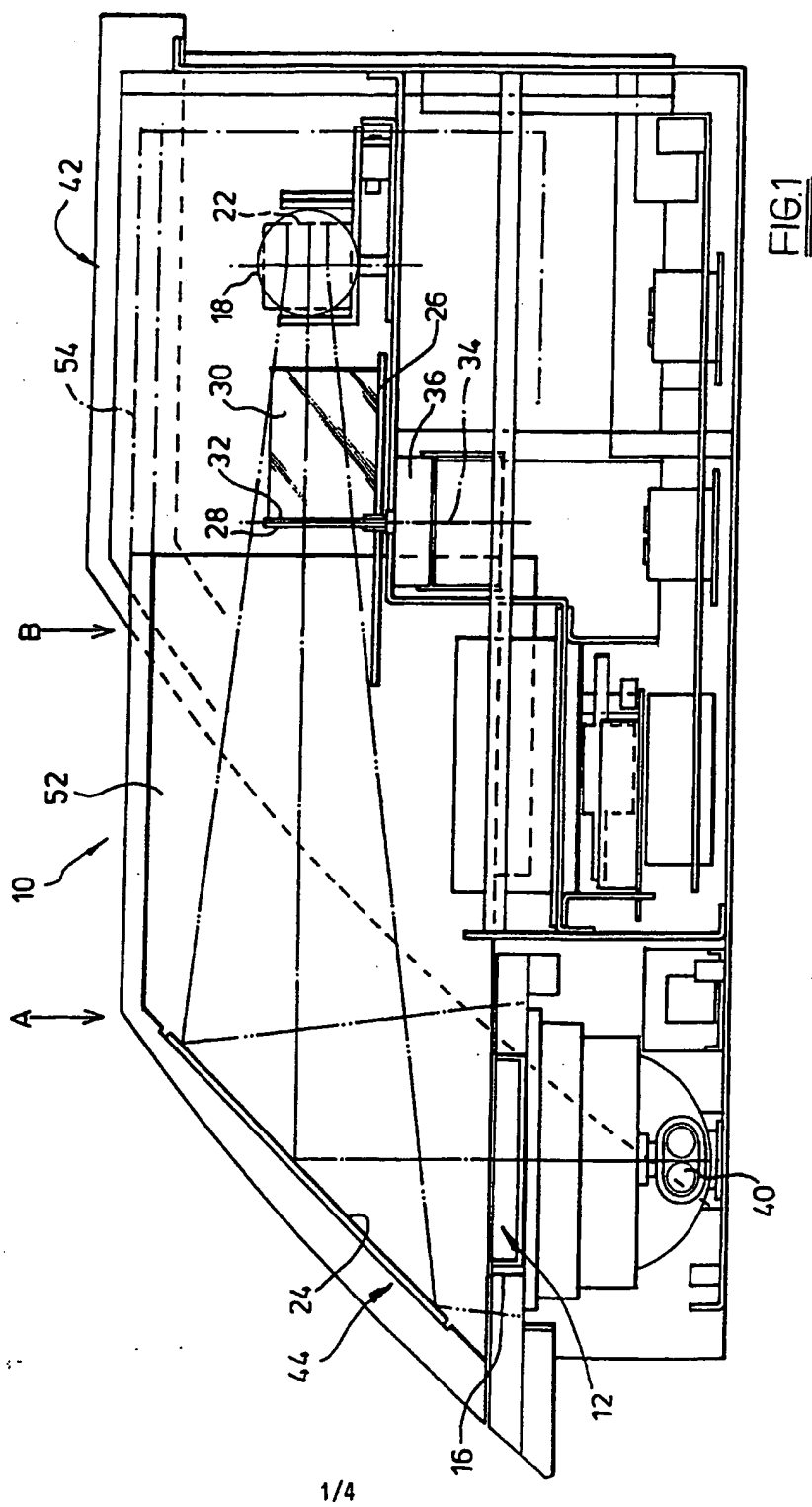
18. Apparatus according to any one of preceding claims 15 to 17 wherein said colour filter means are mounted on an indexable carousel.

19. Apparatus according to any one preceding claim from 15 to 18 wherein there are three colour filter means.

20. Apparatus according to claim 19 wherein said colour filter means comprise red, green and blue.

21. Apparatus according to any one of preceding claims 15 to 20 wherein said sample image comprises a sample tray having a plurality of individual sample wells, said sample tray being held stationary in said sample image receiving means and being viewed by said camera by moveable mirror means which are indexable between positions to allow placement and removal of said sample tray.

22. Apparatus according to any one preceding claims from 15 to 21 further including computer program means for operating said apparatus in a predetermined sequence of operating steps.



**FIG. 1**

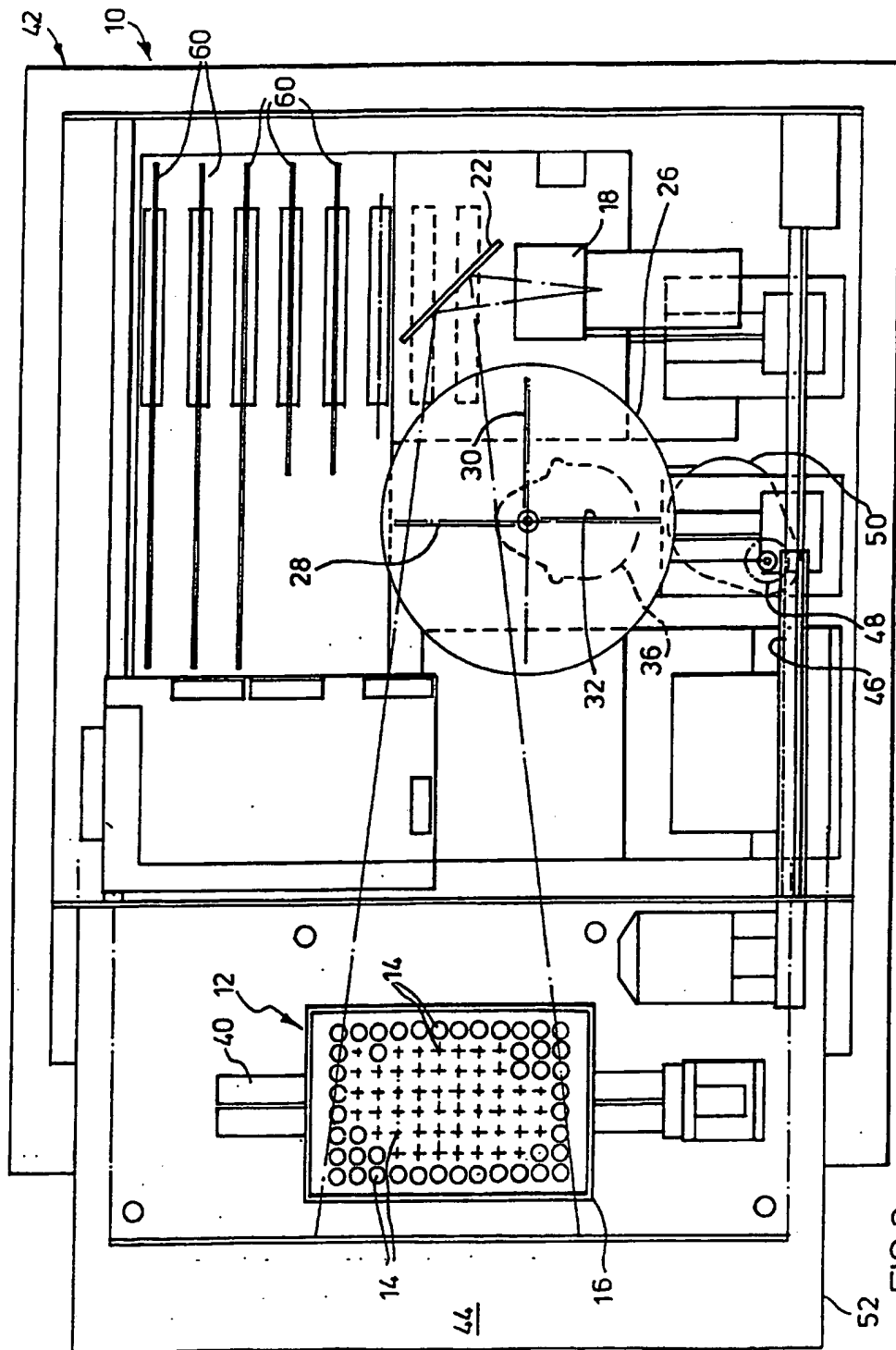


FIG. 2

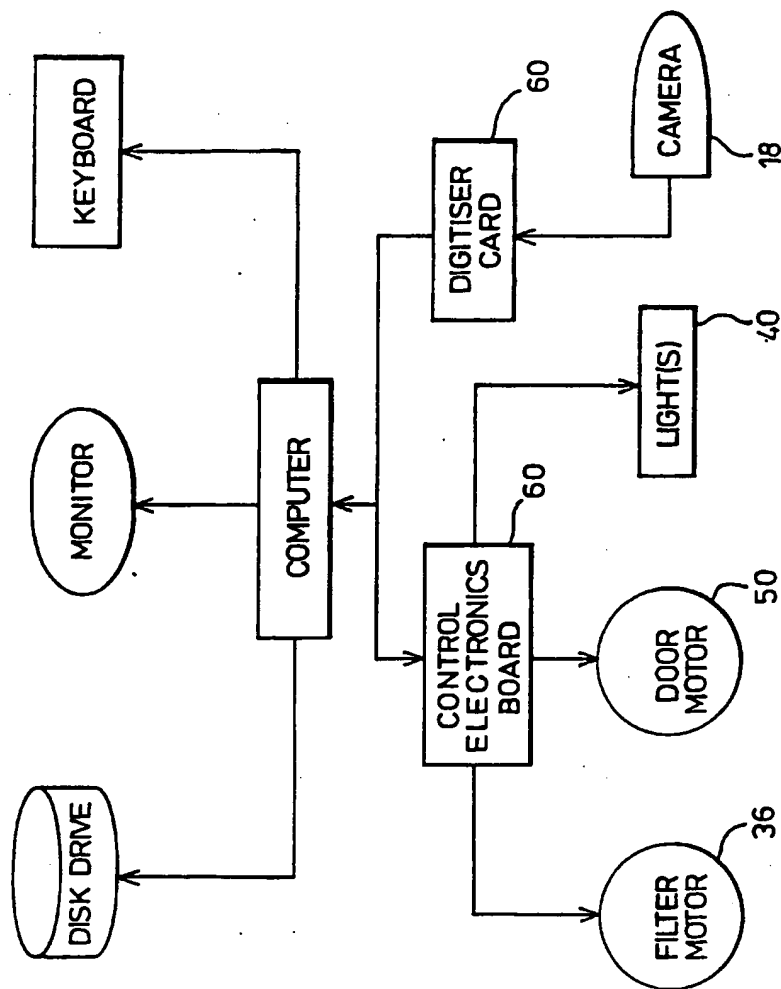
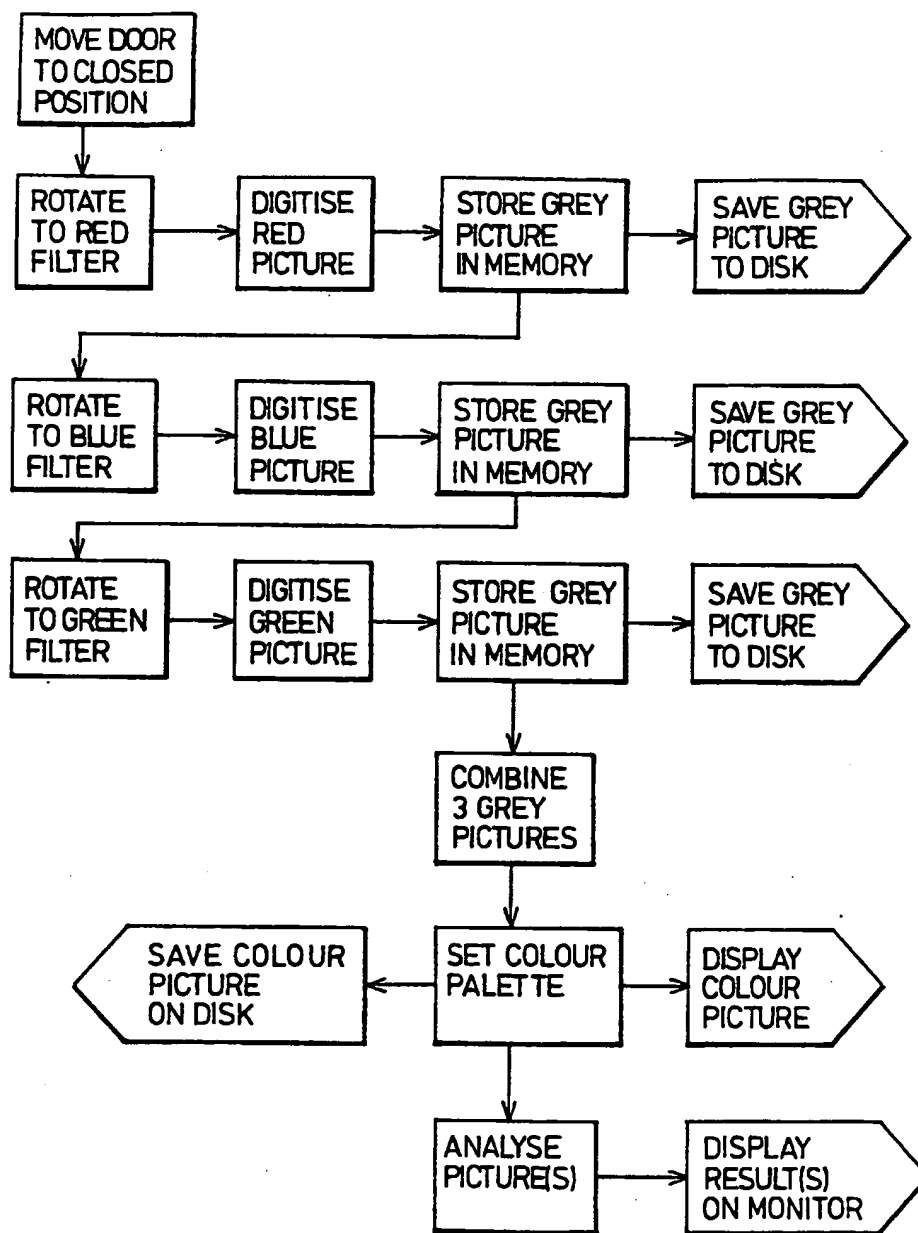


FIG.3

FIG.4

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 93/02262

A. CLASSIFICATION OF SUBJECT MATTER  
 IPC 5 G06F15/70 G01N15/14

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
 IPC 5 G06F G01N

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## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>COMPUTER VISION GRAPHICS AND IMAGE PROCESSING.            vol. 33, no. 3, March 1986, NEW YORK US pages 364 - 376            H.HARMS ET AL. 'combined local color and texture analysis of stained cells'            see page 365, line 4 - line 12            see page 368, paragraph B. - page 371;            figure 6            see page 374, line 7 - line 17</p> <p style="text-align: center;">-/--</p>	<p>1-3, 5-7,            9, 11, 12,            15-17,            19, 20</p>

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Date of the actual completion of the international search

26 January 1994

Date of mailing of the international search report

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>PATTERN RECOGNITION LETTERS vol. 11, no. 1 , January 1990 , AMSTERDAM NL pages 51 - 58 XP84831 I. ANDREADIS ET AL. 'Image pixel identification by chromaticity analysis' see page 51, right column, line 2 - page 52, paragraph 2.2</p> <p>---</p>	<p>1-3,5-7, 9,11,12, 15-17, 19,20</p>
A	<p>PATENT ABSTRACTS OF JAPAN vol. 14, no. 452 (P-1112)27 September 1990 &amp; JP,A,21 081 652 (HITACHI KK) 16 July 1990 see the whole document see abstract</p> <p>-----</p>	<p>1</p>

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